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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 48

Serial Number: 08/909,879
Filing Date: August 12, 1997
Appellant(s): Prieels et al.

Eyal H. Barash
For Appellant

EXAMINER'S ANSWER

This is in response to Appellant's Brief on Appeal filed June 29, 2000, and the Request for Reconsideration filed June 29, 2000.

The Art Unit location of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648.

Applicant's Request for Reconsideration, Paper No. 46, has been considered but is not found persuasive. Applicant has argued that a reference, Joag, *Primate Models of AIDS, Microbes and Infection*, 2, 2000, 223-229 overcomes the rejection. No copy of the reference was found attached to the Request for Reconsideration. However, as a copy of the reference was found in Appellant's Exhibit Book attached to the Brief on Appeal, the Examiner has considered the reference. The Examiner's response is incorporated in the Examiner's Answer set forth below.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims.

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention.

The summary of invention contained in the brief is correct.

(6) Issues.

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims.

The Examiner concurs with appellant's statement that the claims stand or fall together.

(8) Claims Appealed.

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

FAHEY et al., "Status of immune-based therapies in HIV infection and AIDS," *Clin. Exp. Immunol.* 88:1-5, 1992.

Fox, J. L., "No Winner Against AIDS," *Bio/Technology* 12:128, February, 1994.

Haynes et al., "Update on the Issues of HIV Vaccine Development," *Ann. Medicine* 28:39-41, 1996.

Cohen, J., "Jitters Jeopardize AIDS Vaccine Trials," *Science* 262:980-981, 12 November 1993.

Butini et al., "Comparative Analysis of HIV-Specific CTL Activity in Lymphoid Tissue and Peripheral Blood," *J. Cell. Biochem.* Supplement 18B, Abstract No. J306, 1994.

(10) Grounds of Rejection.

The following ground(s) of rejection are applicable to the appealed claims.

Claims 19-20 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claimed invention is directed to vaccine compositions to protect against infection by Human Immunodeficiency Virus (HIV) and a method of making the claimed vaccine composition. However, the specification does not provide sufficient guidance to allow one skilled in the art to make and use the claimed invention with a reasonable expectation of success and without undue experimentation. Applicant's specification sets forth no convincing evidence of vaccine efficacy with respect to HIV. Rather, Applicant relies upon the declarations of Dr. Gerald Voss, Paper Nos. 28 and 33, which provide evidence of protection in the SHIV rhesus monkey animal model.

It is well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein; 2) the fact that

the modes of viral transmission include both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission; 3) the existence of a latent form of the virus; 4) the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier; and 5) the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation.

It is well known in the art that individuals infected with HIV produce neutralizing antibodies and cell mediated responses to the virus, yet these immune responses are not protective and do not prevent the infection from progressing to its lethal conclusion. Further, as taught by Fahey et al., clinical trials using a variety of immunologically based therapies have not yielded successful results in the treatment and/or prevention of HIV infection (see Table 1). The failure of all immune-system-boosting therapies for treating AIDS is further discussed by Fox. The teachings of Fahey et al. and Fox are further confirmed by Haynes et al.. Haynes et al. teach the major scientific obstacles blocking development of HIV vaccines (see page 40, first column, second full paragraph). Further, Haynes et al. teach that "Current animal models of either HIV or simian immunodeficiency virus (SIV) fall short of precisely mirroring human HIV infection" and that "lacking these models, researchers must turn towards human clinical trials to answer many of the difficult questions about HIV pathogenesis and HIV vaccine development" (see page 40, first column, third full paragraph). Thus, it is clear from the evidence of Fahey et al., Fox, and Haynes et

al. that the ability to treat and/or prevent HIV infection is highly unpredictable and has met with very little success.

The Court has indicated that "inherent in the concept of the 'standard experimental animal' is the ability of one skilled in the art to make the appropriate correlations between the results actually observed with the animal experiments and the probable results in human therapy." *In re Hartop*, 135 USPQ 412 at 426 (CCPA 1962). To date, no HIV vaccine has been shown to be effective in humans and, therefore, one skilled in the art can not make the appropriate correlations between animal models of HIV and the probable results in human therapy as required by the courts. This lack of correlative animal models is precisely the point of the statement by Haynes et al. that "lacking these models, researchers must turn towards human clinical trials to answer many of the difficult questions about HIV pathogenesis and HIV vaccine development." Since no animal model of HIV infection is known to reasonably correlate with *in vivo* efficacy in humans, Applicant's reliance on the evidence of Dr. Voss is insufficient to overcome the rejection.

The unpredictability of HIV vaccines is further evidenced by the teachings of Cohen, *Science* 262:980-981, 1993, and Butini et al., *J. Cell. Biochem.*, Suppl. 18B, Abstract J306, 1994. These references have been discussed in depth by the previous Examiner in preceding Office Actions (see, for example, Paper No. 4, paragraph bridging pages 5-6).

It is noted that almost 20 years have elapsed since the identification of the Acquired Immunodeficiency Syndrome (AIDS), more than 15 years since the isolation of HIV-1 and six years since Applicants' filing of their first U.S. application. Considerable resources have been expended

throughout that time to find a suitable vaccine for HIV and yet, despite this monumental effort, no such vaccine has as yet been shown to be effective in humans. While several clinical trials are currently in progress, there is no clear indication of a successful vaccine.

Applicants have not provided any convincing evidence that their claimed invention is indeed useful as a therapeutic or preventative for HIV infection and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

(11) Response to Argument.

Appellant has argued that the Examiner should be reversed for three reasons: 1) the Examiner did not meet his burden to establish a *prima facie* case; 2) the Examiner's evidence is outdated and irrelevant; 3) appellant's evidence establishes enablement of the claimed invention (see Brief, page 5, first full paragraph). The Examiner will address these arguments in turn.

The Examiner has met his burden.

Appellant argues that Haynes et al. is irrelevant as appellants do not rely on the chimpanzee animal model (see Brief, page 12, second full paragraph). This is not persuasive. The evidence of Haynes et al. is not limited to the chimpanzee animal model. Haynes et al. is a highly relevant review of the state of the art of vaccine development for HIV. Further, to the extent that Haynes et al. does discuss the chimpanzee animal model, appellant's own evidence discloses that the chimpanzee model is a

more biologically relevant animal model for HIV than either the SHIV/macaque model used by appellant or the SIV/macaque model also favored by some researchers (see Joag, Appellant's Exhibit 8, page 227, paragraph bridging columns 1-2). And yet, even with the higher biological relevance of the chimpanzee model, the conclusions of Haynes remains clear: "Current animal models of either HIV or simian immunodeficiency virus (SIV) fall short of precisely mirroring human HIV infection" and that "lacking these models, researchers must turn towards human clinical trials to answer many of the difficult questions about HIV pathogenesis and HIV vaccine development" (see page 40, first column, third full paragraph).

Appellant further argues with respect to the Examiner's burden that the Examiner's arguments regarding the complexities and difficulties associated with HIV are insufficient to prove non-enablement (see Brief, pages 13-15). This is not persuasive. Appellant's position on this matter is completely untenable. The complexities and difficulties associated with HIV directly impact the unpredictability of making and using HIV vaccines. This extreme unpredictability is clear from twenty years of AIDS research and, in the absence of convincing objective evidence to the contrary, would not allow one skilled in the art to make and use the claimed vaccines and method with a reasonable expectation of success and without undue experimentation.

The Examiner's Evidence is Relevant

Appellants argue that the Examiner's evidence is irrelevant and outdated and that the Examiner has failed to challenge the SHIV/macaque model used by Appellant and ignored the declaration evidence of Voss and the teachings of Joag and Mooij. In addition, Appellant argues that the Examiner has placed an unfair burden on appellants (see Brief, pages 15-18). This is not persuasive.

Again, appellants' position is untenable. To state that the Examiner has failed to challenge appellants' SHIV/macaque model is to ignore the existence of the outstanding rejection. The Examiner's rejection under 35 U.S.C. § 112, first paragraph, is a direct challenge of appellants' animal model data. It is the Examiner's position that not only cannot appellants' animal model be shown to reasonably correlate with *in vivo* efficacy in humans, but that, to date, no animal model for HIV vaccines has shown to correlate with efficacy in humans. No one has yet to successfully show that humans can even be vaccinated against HIV infection. Twenty years after discovery of the virus, there is still no clear consensus among researchers as to what should even be considered a strong candidate for vaccine trials. This is not information limited to those skilled in the art. AIDS vaccine research is the subject of the nightly television news programs. Even those of no skill in the art are keenly aware via the media that research has yet to provide a vaccine for AIDS. Appellants would have the Examiner ignore twenty years of difficult and painful research into AIDS vaccine so that Appellants could obtain exclusive rights based on limited animal model data. Such a position ignores the requirements of 35 U.S.C. § 112, first paragraph, which clearly places the burden on appellant to provide a specification which enables one skilled in the art to make and use the claimed invention without undue experimentation. It is not an unfair burden on appellant to provide an enabling disclosure, it is a statutory burden.

The Examiner's evidence is highly relevant and has not gone out of date. The conclusions of Haynes et al., published in 1996, remain valid today. There are many researchers working hard with many *in vitro* and *in vivo* systems and animal models trying to find answers to a terrible viral infection. In spite of the magnitude of the effort, the fact remains that there is still no vaccine for AIDS and no way to correlate an animal model to human efficacy

because there is no evidence yet of what is effective in humans as a vaccine for AIDS.

Appellants' Evidence Does Not Overcome the Rejection.

Appellants argue that their affirmative evidence of the declarations of Voss and the teachings of Mooij and Joag are sufficient to overcome the rejection (see Brief, pages 18-25). This is not persuasive.

Appellants' affirmative evidence all relate to the use of the SHIV/macaque animal model as a suitable animal model for AIDS. This is the arguments relating to the declarations of Voss and the references of Mooij and Joag referred to by Appellants. However, none of Appellants' evidence establishes a correlation between the results in the animal model and *in vivo* efficacy in humans. As set forth by the courts, such a correlation is required for the use of an animal model to support *in vivo* efficacy in humans. As stated during prosecution, the Court has indicated that "inherent in the concept of the 'standard experimental animal' is the ability of one skilled in the art to make the appropriate correlations between the results actually observed with the animal experiments and the probable results in human therapy." *In re Hartop*, 135 USPQ 412 at 426 (CCPA 1962). At this point in time no such correlations have been made because no efficacy in humans has been shown that the animal model(s) could correlate with. Even Appellants' own rebuttal evidence bears out the Examiner's position. Joag concludes that "While no individual model meets all the criteria for an ideal model, the available primate models **collectively** constitute a powerful tool to address almost any question in AIDS research" (see Appellant's Exhibit 8, page 227, paragraph bridging columns 1-2, last sentence). So even Joag, so heavily relied upon by Appellants, concludes that 1) no animal model meets all the criteria for an ideal animal model; 2) it takes all the primate

models used collectively to provide a powerful tool for AIDS research; and 3) even using the collective animal models together, not all questions in AIDS research can be answered using the animal models. This is exactly the Examiner's point. Many researchers are using many different animal models for studying HIV. Many researchers have their own particularly favorite animal models. Yet, none of these animal models to date have been shown to effectively correlate with efficacy in humans. Therefore, it is the Examiner's position that Appellants' reliance on the data from a single animal model, the SHIV/macaque model, is insufficient to allow one skilled in the art to make and use the vaccines and method of the claimed invention with a reasonable expectation of success and without undue experimentation.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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January 16, 2001

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